

### **Remarks/Arguments**

Claims 2, 3, 6, 26, 28 and 29 are cancelled. Claims 8-18 and 25 are withdrawn as being drawn to a non-elected invention. Claims 1, 7, 19, 22 and 27 are currently amended to place them in better form for allowance. Claims 1, 4, 5, 7, 19-24, and 27 remain in the application. Full support for the amendments is found at page 1, lines 13-15, and pages 4, 5 and 6 of the specification.

#### **The 102(b) rejection:**

Claims 1-7, 19-20, 22, 26-27 stand rejected under 35 U.S.C. 102(b) as being anticipated by Dunn, R. L. (U.S. patent 6,120,789). Applicants respectfully traverse the rejection.

Applicants' invention is broadly embodied in currently amended claim 1 which reads:

An orally administered testosterone delivery system with sustained release properties comprising at least one lipid, dry particles containing testosterone, and at least one filler, wherein the dry particles are continuously coated by the lipid and form a homogeneous suspension with the lipid, wherein the system is suitable for oral ingestion, and wherein one dose of the system delivers an effective dose of testosterone as measured by total serum testosterone in the range of about 250 to 1100 ng/dL for greater than about 7 hours.

Claim 1 has been amended from reading, "An orally administered testosterone delivery system" to include, "... suitable for oral ingestion" to more clearly claim the invention. The clarification is such that the present invention is clearly distinguished from that of Dunn (US patent 6,120,789), which is a medical device for implantation (see abstract and claim 1 of Dunn). The present invention is a device for oral ingestion, as indicated in the specification at page 1, lines 13-15 which read, "Before orally administered drugs enter the general circulation of the human body, they are absorbed into the capillaries and veins of the upper gastrointestinal tract and are transported by the portal vein to the liver." The testosterone delivery system is orally ingested, and the testosterone absorbed into the blood stream in the gastrointestinal tract and transported by the portal vein to the liver. In the controls and examples of the invention, the

dogs were given their placebo or test article immediately before being fed (see Example 1). They were fed the placebo or test article, and then their serum levels of testosterone were monitored.

An orally ingested delivery system is clearly distinguished from that of Dunn, which is implanted. When it is implanted to treat periodontal disease, it is still not orally ingested, and is therefore not absorbed in the gastrointestinal tract, as is the present invention.

The problem addressed in the present invention is that of orally ingesting testosterone. The generally accepted medical view is that testosterone cannot be administered by oral ingestion, because after the testosterone is absorbed through the gastrointestinal tract into the blood stream, it passes through the liver via the hepatic portal vein. It is generally believed that the liver destroys the testosterone, so the serum levels of testosterone are not increased by oral ingestion of testosterone. It was surprising, then, to find that the present delivery system increased serum levels of testosterone, and further, that the present delivery system provided sustained release properties.

Dunn discloses the use of a medical device to provide sustained release properties of implanted biologically active agents. Examiner has pointed out, at page 4, second full paragraph of his Office Action, that Dunn's device is suitable for delivering testosterone. Since Dunn's device is not orally ingested, and thought to be destroyed by the liver, one would expect it to be able to deliver testosterone. Dunn is not addressing the problem addressed by the present invention, because it is known that testosterone can be administered transdermally or parentally, as Dunn is doing. The challenge is to administer testosterone via oral ingestion with sustained release properties. Applicants have found a composition that accomplishes that, and that has the unexpected results that led to the present invention.

In view of the above amendments and arguments, Applicants request that the 102(b) rejection of the claims be withdrawn, and that the claims be allowed.

**The 103(a) Rejection:**

Claims 1-7, 19-24 and 26 are rejected under 35 U.S.C.103(a) as being unpatentable over Jain et al. (U.S. patent application 2002/0012675). Applicants respectfully traverse the rejection.

Jain et al. disclose a nanoparticulate controlled release tablet for drug delivery (see paragraphs 0077 to 0083). The present invention, as currently claimed, is a lipid suspension. The dosage is formed by pouring or molding the suspension.

The composition disclosed by Jain et al. is a controlled release nanoparticulate formulation tablet comprising a nanoparticulate agent (drug), a surface stabilizer (surfactant) and a rate-controlling polymer. The nanoparticles have an effective average particle size of less than about 1000 nm. The rate-controlling polymer includes waxes, shellac, and hydrogenated vegetable oils, among many other polymers (see paragraph [0056]).

Jain et al. disclose a controlled release composition that is a tablet or multiparticulate form. Every example give is in a tablet form. Further the importance of the hardness of the tablet is taught at paragraph [0067], stating, "Other than selection of one or more rate-controlling polymers, hardness of the tablet is the factor which contributes most to extended controlled release of the administered agent." In Example 3, three separate hardnesses were tested simultaneously. The results were shown in Fig. 2, which demonstrate that as the hardness of a tablet increases, the controlled release characteristic of the tablet also steadily increase.

Applicants' invention is that of a lipid suspension. It is impossible to tablet such a suspension, which can be molded or enclosed in a gel capsule, because of the flow properties of a lipid suspension, nor can it be formed into discrete particles. Jain et al., in Example 6, used 20% hydrogenated vegetable oil in his composition. Even with that amount of oil, the composition was in the form of a tablet with a hardness of 20-22 kPa. Such a tablet is not contemplated in the present invention.

As to Jain et al. pertaining to hormone therapy, Applicants respectfully point out that the device of Jain et al. can be administered "orally, rectally, buccally or via the vagina" (see paragraph [0085]). Since oral ingestion of testosterone is known to be ineffective for the reasons presented above, other forms of administration, i.e., rectally, buccally or via the vagina, would be used. Clearly the present invention is distinguished from the disclosure of Jain et al.

A full reading of Jain et al. fails to provide or suggest a lipid suspension composition that provides orally ingested testosterone with sustained release properties.

In view of the above amendments and arguments, Applicants request that the 103(a) rejection of the claims be withdrawn, and that the claims be allowed.

#### **The Nonstatutory Obviousness-type Double Patenting Rejection**

Claims 1-7, 19-24 and 26-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,12-19,21 of Us. Patent No. 6,541,025.

Applicants will to submit a terminal disclaimer upon receipt of a Notice of Allowance of the claims.

Applicant looks forward to working with Examiner to resolve any remaining issues in the application. If Examiner has any questions or the Applicant can be of any assistance, Examiner is invited and encouraged to contact the undersigned. If there are any other issue that could be handled by Examiner's Amendment, Examiner is requested to telephone the undersigned.

The Commissioner is authorized to charge any necessary fees or credit any overpayment to Account No. 07-1985.

Respectfully submitted,

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